

CLAIMS: What is claimed is:

1. A composition comprising a glycosylated interferon-beta coupled to a non-naturally-occurring polymer, said polymer comprising a polyalkylene glycol moiety.
2. The composition of claim 1, wherein the polyalkylene moiety is coupled to the interferon-beta by way of a group selected from an aldehyde group, a maleimide group, a vinylsulfone group, a haloacetate group, plurality of histidine residues, a hydrazine group and an aminothioli group.
3. The composition of claim 1, wherein the glycosylated interferon-beta is interferon-beta-1a and is more active than interferon-beta-1b when measured in an antiviral assay.
4. The composition of claim 3, wherein the interferon-beta-1a retains 0.5 to 1 times the potency of interferon-beta-1a lacking said polymer, as measured in an antiviral assay.
5. The composition of claim 1, wherein the interferon-beta is an interferon-beta-1a fusion protein.
6. The composition of claim 5, wherein the interferon-beta-1a fusion protein comprises a portion of an immunoglobulin molecule.
7. The composition of claims 1 or 5, wherein the interferon beta is a mutant interferon beta having at least one of the following properties: (a) the mutant has a higher antiviral activity than wild type inteferon-beta-1a, wherein the antiviral activity is measured by viral induced lysis of cells; (b) the mutant has, relative to wild type interferon-beta-1a, greater antiviral activity than antiproliferative activity; (c) the mutant binds interferon receptor but has, when compared to wild type interferon-beta-1a, lowered antiviral activity and lowered antiproliferative activity relative to receptor binding activity.
8. A physiologically active interferon-beta composition comprising a physiologically active interferon-beta 1a coupled to a polymer comprising a polyalkylene glycol moiety, wherein the physiologically active interferon-beta 1a and the polyalkylene glycol moiety are arranged such that the physiologically

active interferon-beta 1a in the physiologically active interferon-beta composition has an enhanced activity relative to physiologically active interferon-beta 1b, when measured by an antiviral assay.

9. The composition of claim 8, wherein the interferon-beta-1a is coupled to the polymer at a site on the interferon-beta-1a that is an N-terminal end.
10. The composition of claim 8, wherein the interferon-beta-1a is coupled to the polymer at a site on the interferon-beta-1a that is at or near the C-terminal end.
11. ~~The composition of claim 8, wherein the interferon-beta-1a is coupled to the polymer at a site by way of a glycan moiety of the interferon-beta-1a.~~
12. ~~The composition of claim 8, wherein the interferon-beta-1a is an interferon-beta-1a fusion protein.~~
13. The composition of claim 12, wherein the interferon-beta-1a fusion protein comprises a portion of an immunoglobulin molecule.
14. The composition of claims 8 or 12, wherein the interferon-beta-1a is a mutant interferon-beta-1a having at least one of the following properties: (a) the mutant has a higher antiviral activity than wild type inteferon beta 1a, wherein the antiviral activity is measured by viral induced lysis of cells; (b) the mutant has, relative to wild type interferon-beta-1a, greater antiviral activity than antiproliferative activity; (c) the mutant binds interferon receptor but has, when compared to wild type interferon-beta-1a, lowered antiviral activity and lowered antiproliferative activity relative to receptor binding activity.
15. A physiologically active interferon-beta composition comprising a physiologically active glycosylated interferon-beta N-terminally coupled to a polymer comprising a polyalkylene glycol moiety, wherein the physiologically active interferon-beta and the polyalkylene glycol moiety are arranged such that the physiologically active interferon-beta in the physiologically active interferon-beta composition has substantially similar activity relative to physiologically active interferon-beta lacking said moiety, when measured by an antiviral assay.
16. The composition of claim 15, wherein the interferon-beta is coupled to the polymer at a site on the interferon-beta that is an N-terminal end.

17. The composition of claim 15 wherein the interferon-beta is coupled to the polymer at a site on the interferon-beta that is at or near the C-terminal end.
18. The composition of claim 15, wherein the interferon-beta is coupled to the polymer at a site by way of a glycan moiety on the interferon-beta.
- 5 19. The composition of claim 15, wherein the interferon-beta is an interferon beta fusion protein.
20. The composition of claim 19, wherein the interferon beta fusion protein comprises a portion of an immunoglobulin molecule.
- 10 21. The composition of claims 15 or 19 wherein the glycosylated interferon beta is a mutant interferon beta having at least one of the following properties: (a) the mutant has a higher antiviral activity than wild type interferon beta 1a, wherein the antiviral activity is measured by viral induced lysis of cells; (b) the mutant has, relative to wild type interferon-beta-1a, greater antiviral activity than antiproliferative activity; (c) the mutant binds interferon receptor but has, when compared to wild type interferon-beta-1a, lowered antiviral activity and lowered antiproliferative activity relative to its receptor binding activity.
- 15 22. A stable, aqueously soluble, conjugated interferon-beta 1a complex comprising a interferon-beta 1a coupled to a polyethylene glycol moiety, wherein the interferon-beta 1a is coupled to the polyethylene glycol moiety by a labile bond, wherein the labile bond is cleavable by biochemical hydrolysis and/or proteolysis.
- 20 23. A interferon-beta composition according to claims 1, 15 or 22, wherein the polymer has a molecular weight of from about 5 to about 40 kilodaltons.
24. A pharmaceutical composition comprising the interferon-beta composition of claim 23.
- 25 25. A method of treating a potential or developed condition or disease state in a mammalian subject with a interferon-beta 1a effective therefore, comprising administering to the subject an effective amount of an interferon-beta 1a composition comprising said interferon-beta 1a coupled to a polyethylene glycol moiety.
- 30 26. The method of claim 25, wherein the interferon-beta-1a is coupled to the polymer at a site on the interferon-beta-1a that is an N-terminal end.

27. The method of claim 25, wherein the interferon-beta-1a is coupled to the polymer at a site on the interferon-beta-1a that is at or near the C-terminal end.
28. The method of claim 25, wherein the interferon-beta-1a is coupled to the polymer at a site by way of a glycan moiety on the interferon-beta-1a.
- 5 29. The method of claim 25, wherein the interferon-beta-1a is an interferon-beta-1a fusion protein.
30. The method of claim 29, wherein the interferon-beta-1a fusion protein comprises a portion of an immunoglobulin molecule.
31. The method of claims 25 and 29, wherein the interferon-beta-1a is a mutant
10 interferon-beta-1a having at least one of the following properties: (a) the mutant has a higher antiviral activity than wild type inteferon beta 1a, wherein the antiviral activity is measured by viral induced lysis of cells; (b) the mutant has, relative to wild type interferon-beta-1a, greater antiviral activity than antiproliferative activity; (c) the mutant binds interferon receptor but has, when
15 compared to wild type interferon-beta-1a, lowered antiviral activity and lowered antiproliferative activity relative to its receptor binding activity.
32. A method of prolonging the activity of interferon-beta-1a in an in vivo or in vitro system, comprising coupling said interferon-beta 1a to a non-naturally-occurring polymer moiety to yield a coupled polymer-interferon-beta 1a composition, and
20 introducing the coupled polymer-interferon-beta composition to the in vivo or in vitro system.
33. The method of claim 32, wherein the interferon-beta-1a is coupled to the polymer at a site on the interferon-beta-1a that is an N-terminal end.
34. The method of claim 32, wherein the interferon-beta-1a is coupled to the polymer
25 at a site on the interferon-beta-1a that is at or near C-terminal end.
35. The method of claim 32, wherein the interferon-beta-1a is coupled to the polymer at a site by way of a glycan moiety on the interferon-beta-1a.
36. The method of claim 32, wherein the interferon-beta-1a is an interferon-beta-1a fusion protein.
- 30 37. The method of claim 36, wherein the interferon-beta-1a fusion protein comprises a portion of an immunoglobulin molecule.

38. The method of claims 32 and 36, wherein the interferon-beta-1a is a mutant
interferon-beta-1a having at least one of the following properties: (a) the mutant
has a higher antiviral activity than wild type inteferon beta 1a, wherein the
antiviral activity is measured by viral induced lysis of cells; (b) the mutant has,
5 relative to wild type interferon-beta-1a, greater antiviral activity than
antiproliferative activity; (c) the mutant binds interferon receptor but has, when
compared to wild type interferon-beta-1a, lowered antiviral activity and lowered
antiproliferative activity relative to its receptor binding activity.
39. The method of claim 32, wherein the polymer comprises a polyalkylene glycol.
- 10 40. A method of inhibiting angiogenesis in a subject, comprising administering to a
subject an effective amount of the composition of claim 23.